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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/501,065

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Patrick Chesne

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EXAMINER

CROUCH, DEBORAH

ART UNIT

PAPER NUMBER

1632

MAIL DATE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/501,065	Applicant(s) CHESNE ET AL.	
	Examiner Deborah Crouch, Ph.D.	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7-20, 25-33, 38-45 and 51-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-20, 25-33, 38-45 and 51-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 July 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Applicant's arguments filed October 29, 2007 have been fully considered but they are not persuasive. The amendment has been entered. Claims 1-5, 7-20, 25-33, 38-45 and 51-56 are pending.

The IDS filed October 21, 2005 is being provided again as one reference was not previously initialed.

The portion of the rejection made in the office action mailed April 26, 2007 under 35 U.S.C. § 112, first paragraph as lacking enablement for primate mammals is withdrawn.

The rejection of claims 21-24 and 34-37 under 35 U.S.C. 102(b) or, in the alternative, under 35 U.S.C. 103(a) as obvious made in the office action mailed April 26, 2007 has been withdrawn.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7-20, 25-33, 38-45 and 51-56 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a rabbit by nuclear transfer comprising inserting a rabbit donor somatic cell into an enucleated rabbit mammalian oocyte of the same species as the donor cell to produce a nuclear transfer embryo, activating the oocyte cycloheximide and 6-dimethylamino purine to produce a reconstituted embryo, transfer of the reconstituted embryo to the uterus of a 22 hour asynchronous female rabbit, and permitting development of the reconstituted embryo to term, does not reasonably provide enablement for the claims as written for reasons set forth in the office action mailed April 26, 2007. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Neither the specification nor the claims teach or provide a means through which to determine the variable "T" in $t = t_0 + T$ (+/- 25% T). The claims and the specification never discuss determining "T" or providing a value for "T." Without knowing "t" one could not calculate "T." Without "T" one would not know the asynchrony of development between two embryos to determine when after fertilization an embryo should be transferred to the uterus of a recipient female. Further, the specification and the claims do not clearly define "t₀." That is "t₀" is the time of crossing a vasectomized male with a female or the time of crossing a fertile male with a female, each to produce an embryo. However, the specification and the claims do not state exactly what "t₀" measures. Is the hour/minute of mating? Is it the time post-ovulation? More explanation is needed for the variables in the formula for the formula, and the method, to be used. Additionally, the only means taught by the specification to determine "T" is through cell or blastomere counting of the embryos. If one knows the embryo is a one-cell, 2-cell, 4-cell, 8-cell, 16-cell, morula or blastocyst stage embryo, then the determination has been completed.

The claims are further not enabled because claim 1 states "the determination taking place on or before the day of uterine implantation of said second embryo." However, there is no transfer to a uterus step in claim 1(a)(ii). Also, the specification does discuss how to determine asynchrony of development once the embryo has been transferred to the uterus. A transferred embryo may not implant immediately into the uterine wall. It is noted that fertilized eggs do not require artificial or parthenogenetic activation. Sperm entry induces a series of events, one of which is activation of the egg. Also, the method of evaluating would need to transfer an embryo of the same species as those evaluated or the attempt to gain synchrony would be fraught with species differences.

With regards to the asynchrony between oocyte donor rabbit and embryo recipient rabbit, the specification states that transfer of 1-4 cell stage embryos to female results in no

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fetal rabbit development (specification, page 28, parag. [0085]). Further, the specification states NT embryos reach blastocyst stage in vitro just as the zygotes and parthenotes, but the NT embryos at day 4 about one day behind (specification, page 28, parag. [0083]). When 16 hour asynchronous females are used as recipients, the rate of implantation increases, but none of the females remained pregnant (page 29-30, bridg. parag.). Live cloned rabbits were obtained with 22 hour asynchrony (page 30, parag. [0087]). Thus, there is great unpredictability in producing live-born, cloned rabbits. Applicant has been limited to the particular method disclosed in the specification to produce cloned rabbits because insufficient guidance has been provided to determine "t" given the above deficiencies in the formula.

It is noted that claims 43, 44, and 56 encompass cross-species nuclear transfer, by not specifying the reconstituted embryo was transferred to the uterus of a female of the same species, as well as encompass the production of primates by nuclear transfer. At the time of filing, cross-species nuclear transfer and the cloning of primates were not regarded enabled. Meirelles demonstrates that methods of nuclear transfer where the nuclear material of *Bos indicus* is inserted into the oocyte of *Bos taurus* produces calves comprising the nuclear material of *Bos indicus* and the mitochondria of *Bos taurus*. Meirelles *et al.* teach that previous attempts to use the *Bos* oocyte as hosts for nuclear transfer from unrelated species allowed development to the blastocyst stage, and conclude that incompatibility among the nuclear and mitochondrial genetic systems is responsible for the early arrest. Meirelles also points to similar failures using *Mus caroli* and *Mus musculus* citing Dominko. Meirelles concludes that in light of their results and the failures of the prior art, that nuclear transfer across subspecies barriers is possible (see Meirelles, pp. 351-355). In addition, the claims encompass methods of nuclear transfer when the oocyte is off a different species than the surrogate mother animal. Further, in the production of sheep goat chimeras, there

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were biases towards chimeras whose genotype and phenotype was most like that of the recipient, and that the successful production of chimeras resided in the neutralization of incompatibility between the chimeric embryos (Fehilly et al (1985), page 221, parag. 1).

Applicant argues the claims have been amended as suggested by the Examiner. This argument is not persuasive.

The only amendment to the claims related to the enablement rejection is the limitation to "non-primate mammal." The rejections based on cross-species nuclear transfer have not been addressed as well as the rejection based on activation of a sperm fertilized egg.

Applicant argues the specification and the claims define "T" such that "t" can be calculated. However, the rejection is the determination of "T." The specification only discusses blastomere counting. Further, "t₀" is not clear as what "t₀" measures is not clear. It is understood the animals were conceived at the same time, but what "t₀" actually is not evident.

Claims 1-5, 7-20, 25-33, 38-45 and 51-56 because the prior art did not teach or suggest the methods as presently claimed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant

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to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 6:00 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch, Ph.D. /
Primary Examiner, Art Unit 1632

February 26, 2008